PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	23.08.2004
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
031571woMetg	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/06799	27.06.2003	28.06.2002

Applicant
BRAUN, Jan Matthias ET AL.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 031571woMetg	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/06799	International filing date *(day/month/year)* 27.06.2003	Priority date *(day/month/year)* 28.06.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/095		
Applicant BRAUN, Jan Matthias ET AL.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.01.2004	23.08.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Noë, V Telephone No. +31 70 340-4181

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/06799

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-56 as originally filed

Claims, Numbers

1-12 filed with telefax on 14.07.2004

Drawings, Sheets

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-12
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-12
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-12
	No:	Claims	

2. Citations and explanations

   see separate sheet

V. Reasoned statement (Continuation)

1 CITATIONS

Reference is made to the following documents:

D1: JI YIN-DUO ET AL: "The antigen specificity of meningococcal bactericidal antibodies induced by N. lactamica and N. meningitidis." ZHONGHUA WEISHENGQUXUE HE MIANYIXUE ZAZHI, vol. 14, no. 4, 1994, pages 233-237, XP008013995 ISSN: 0254-5101

D2: WO 00/50074 A (GORRINGE ANDREW RICHARD ;HUDSON MICHAEL JOHN (GB); IMP COLLEGE SCH) 31 August 2000 (2000-08-31)

D3: EP-A-0 941 738 (AMERICAN CYANAMID CO) 15 September 1999 (1999-09-15)

D4: FR-A-2 782 642 (FORCEVILLE XAVIER) 3 March 2000 (2000-03-03)

D5: GRIFFISS J M ET AL: "Meningococcal molecular mimicry and the search for an ideal vaccine." TRANSACTIONS OF THE ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE. ENGLAND 1991, vol. 85 Suppl 1, 1991, pages 32-36, XP008013992 ISSN: 0035-9203

2 NOVELTY (Art. 33(2) PCT)

2.1 The subject-matter of claims 1-12 have not been disclosed in the cited prior art and are therefore considered to be novel.

2.2 The present application satisfies the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-12 is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

3 INVENTIVE STEP (Art. 33(3) PCT)

3.1 For inventive step analysis of claim 1, D1 is considered to represent the most

relevant state of the art and discloses the induction of an immune response to Neisseira meningitidis serogroup a in mice by LOS from Neisseria lactamica (see abstract). The subject-matter of claim 1 differs in that a medicament for the treatment or prevention of Neisseria meningitidis infection comprising glycoconjugates and/or lipooligosaccharides (LOS) from Moraxella catarrhalis is claimed.

3.2 The problem to be solved by the subject matter of claim 1 may therefore be regarded as the provision of an alternative medicament for the treatment or prevention of Neisseria meningitidis infection. The solution would be a medicament comprising glycoconjugates and/or lipooligosaccharides (LOS) from Moraxella catarrhalis.

3.3 This solution is considered as involving an inventive step (Article 33(3) PCT) because the prior art does not disclose nor suggests the use of LOS from Moraxella catarrhalis in a medicament for the prevention or treatment of a Neisseria meningitidis infection and it would not be obvious for the person skilled in the art to make such a medicament.

3.4 For inventive step analysis of claim 3, D1 is considered to represent the most relevant state of the art and discloses the induction of an immune response to Neisseira meningitidis serogroup a in mice by LOS from Neisseria lactamica (see abstract). The subject-matter of claim 3 differs in that a medicament for the treatment or prevention of Neisseria meningitidis infection comprising glycoconjugates and/or lipooligosaccharides (LOS) from Neisseria lactamica which are cross-reactive to human blood antigens is claimed.

3.5 The problem to be solved by the subject matter of claim 3 may therefore be regarded as the provision of an alternative medicament for the treatment or prevention of Neisseria meningitidis infection comprising glycoconjugates and/or lipooligosaccharides (LOS) from Neisseria lactamica. The solution would be a medicament comprising glycoconjugates and/or lipooligosaccharides (LOS) from Neisseria lactamica which are cross-reactive to human blood antigens.

3.6 This solution is considered as involving an inventive step (Article 33(3) PCT) because the prior art does not disclose nor suggests the use of LOS from Neisseria lactamica which are cross-reactive with human blood group antigens. On the contrary, D5 would discourage the skilled person to use these LOS antigen

in a medicament for the prevention or treatment of a Neisseria meningitidis infection, since these blood group antigens are potential self-antigens and thus are not involved in the development of immunity against meningococci (see page 32, introduction).

3.7 For the same reasons as indicated above, the subject-matter of claim 12 is considered to be inventive.

3.8 The present application does satisfy the criterion set forth in Article 33(3) PCT and the subject-matter of claims 1-12 involves an inventive step (Rule 65(1)(2) PCT).

Claims

1. A medicament for the treatment or prevention of diseases due to infection by *Neisseria meningitidis*, characterized in that it comprises

   glycoconjugates and/or lipooligosaccharides (LOS) purified or included in outer membrane vesicles, blebs, lipid layers, liposomes and/or killed bacteria from commensal *Moraxella catarrhalis* with cross-reactive antigens to *Neisseria meningitidis* of the serogroup A, B, C, H, I, K, L, X, Y, Z, 29E or W135, or non-capsulated meningococcal strains,

   and/or antibodies against such glycoconjugates and/or lipooligosaccharides.

2. The medicament of claim 1, wherein the cross-reactive antigens to *Neisseria meningitides* are oligosaccharides of LOS, which are cross-reactive with human blood group antigens.

3. A medicament for the treatment or prevention of diseases due to infection by *Neisseria meningitides*, characterized in that it comprises

   glycoconjugates and/or lipooligosaccharides (LOS) purified or included in outer membrane vesicles, blebs, lipid layers, liposomes and/or killed bacteria from commensal *Neisseria lactamica* with cross-reactive antigens to *Neisseria meningitides* of the serogroup B, C, H, I, K, L, X, Y, Z, 29E or W135, or non-capsulated meningococcal strains, wherein the cross-reactive antigens to *Neisseria meningitides* are oligosaccharides of LOS, which are cross-reactive to human blood group antigens, and/or antibodies against such oligosaccharides of LOS.

4. The medicament of claim 1 or 3, characterized in that the glycoconjugates and/or lipooligosaccharides are chemically modified, conjugated and/or hydrolyzed, preferably by mild acid hydrolysis.

5. The medicament of claim 1 or 3, preferably for the treatment of acute meningitis or septicaemia, characterized in that the antibodies are monoclonal or polyclonal, and that they are obtained from commensal and/or meningococcal species from:

- virus immortalized human lymphocytes secreting the glycoconjugate neutralizing, specific or cross-reactive antibodies,
- from human lymphocytes secreting the neutralizing antibodies fused with a human hybridoma cell line,
- from immunized animals, preferably mice, rats, rabbits or pigs producing polyclonal serum against such antibodies, or
- from immunized animals, preferably mice, rats, rabbits or pigs, after fusion of the mouse lymphocytes with a human or animal hybridoma cell line.

6. The medicament of claim 1 or 3, characterized in that it is a vaccine.

7. The medicament of claim 1 or 3, characterized in that it is provided as a nasal/oral spray, as a liquid for injection, as an orally applied capsule or tablet and/or in combination with an adjuvant.

8. The medicament of claim 1 or 3 for the treatment of acute meningitis or septicaemia, and/or passive immunisation and/or protection of close contacts and/or susceptible individuals, characterized in that the antibodies are monoclonal or polyclonal, and that they are obtained from commensal and/or meningococcal species, and/or native and/or toxin-conjugated, and/or adjuvant supplemented human blood group antigens (sialylated and non-sialylated forms of P, pK, paragloboside, Ii, Lewis):
   - from virus immortalized human lymphocytes secreting the glycoconjugate neutralizing, specific and/or cross-reactive antibodies
   - isolated from human serum and/or plasma, and/or human breast milk, and/or human secretions (i.e saliva),
   - from human lymphocytes secreting the neutralizing antibodies,
   - from human lymphocytes secreting the neutralizing antibodies fused with a human or animal hybridoma cell line,
   - from immunized animals, preferably mice, rats, rabbits, or pigs producing polyclonal serum against such antigens, or

- from immunized animals, preferably mice, rats, rabbits, or pigs after fusion of the animal lymphocytes with a human or animal hybridoma cell line.

9. The medicament of any one of the claims 1 to 8, characterized in that the antibodies are of the classes IgA_1, IgA_2, IgD, IgG_1, IgG_2, IgG_3, IgG_4, IgM, and/or IgE, that are secreted and/or membrane bound to human or animal cells, and/or to artificial membranes and/or liposomes.
10. The medicament of any one of the claims 1 to 9 for passive immunisation, characterized that it is provided as a nasal, oral or mucosal spray and/or tincture, as a liquid for injection, as an orally applied capsule or tablet and/or in combination with sodium selenite and/or with an adjuvant.
11. The medicament for passive immunisation with antibodies of any one of the claims 1 to 10, characterized that it is applied in combination with or without sodium selenite, or that sodium selenite is used as an agent for the treatment and/or protection of meningococcal disease without the medicament of claim 4, and/or prior to the application of the medicament of claim 4, and/or parallel to the application of the medicament of claim 4, and/or after to the application of the medicament of claim 4.
12. A diagnostic to assess the susceptibility of patients for diseases due to *Neisseria meningitidis*, characterized in that it comprises glycoconjugates and/or lipooligosaccharides from commensal bacteria with cross-reactive antigens to *Neisseria lactamica* or *Moraxella catarrhalis* and/or antibodies against such glycoconjugates and/or lipooligosaccharides and/or oligosaccharides of LOS of any of the claims 1 to 11.